**REMARKS**

Applicant has amended claim 1 to add the term "and" between the steps (a) and (b). As such the amendment is clerical and its entry is respectfully requested.

Applicant notes for the record that the Restriction Requirement issued on December 23, 2003, that the claims were allegedly generic to a plurality of disclosed patentability distinct species comprising an inhibitor that specifically inhibits Type 4 cyclic adenosine monophosphate diesterases was withdrawn in the Office Action mailed on November 1, 2004 based upon the Applicant's arguments made of record in the response to the Restriction Requirement mailed on April 21, 2004.

The Examiner rejected claims 1-7 and 16 as allegedly not complying with 35 U.S.C. 112, first paragraph, written description requirement. The Examiner contends that in the specification only two specific inhibitors of Type 4 adenosine monophosphate phosphodiesterase are disclosed in the specification, namely Rolipram and 4 – (3 – Butoxy – 4 – methoxybenzyl) – 2 – imidazolidinone (XX5). The Examiner argues that written description requirement of the claims is not met because the specification allegedly does not contain "any structural characteristics, chemical formula, name(s) or physical properties, aside from the express identification of the two compounds, which would provide adequate written description of the genus of compounds capable of specifically inhibiting Type 4 adenosine monophosphate phosphodiesterases."

Applicant respectfully disagrees and submits that the rejection should be withdrawn for the following reasons.

The specification provides a detailed written description of the class of PDE4 specific inhibitors. See for example, page 4, lines 6 – 13; page 6, line 15; page 7 – line 13.The specification provides a detailed explanation of what the class of inhibitors is. It provides examples of compounds falling within the class and a compound that is not part of the class. Citations to publications further exemplifying this are also provided. The key to remember is that this is not a class of compounds that is unknown, but rather, at the time of filing, was a known class of compounds.

Moreover, the pending claims are not directed to compounds per se. The claims are directed to methods for treating CLL using specific PDE4 inhibitors. The Examiner cites *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d. 1559 (Fed. Cir. 1997) in alleging that "adequate written description requires precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plain [sic] for obtaining **the claimed chemical invention**" (page 3, 2nd full par. of October 31, 2007 Office Action, emphasis added). *Regents of the University of California v. Eli Lilly & Co.* dealt with claiming an unknown compound. However, in Lily, the compound was unknown. That is not what is claimed here. What Applicant claims is the **use of a known class of compounds, PDE4 specific inhibitors, in treating CLL**. Thus, Lily is not pertinent. The Federal Circuit has specifically dealt with the difference between claiming a class of unknown compounds and claiming a method of **using known compounds** in *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005) (attached herewith). It is that latter situation the present claims are dealing with.

Applicant submits herewith a 2nd Lerner Declaration under 37 C.F.R. 1.132 executed by Dr. Adam Lerner ("2nd Lerner Declaration").

As stated by Dr. Lerner, prior to the filing date, September 24, 1998, the term "specific PDE4 inhibitor" was well known: A number of other specific PDE4 inhibitors were well known to a skilled artisan. For example, compounds RP73401, LAS31025, SB207499, and CDP840, CP80633, CP77059BRL61063, denbufylline, and MNS949 were all known to the skilled artisan as specific PDE4 inhibitors. It was also known what defines a specific PDE4 inhibitor. It has further been well known that different forms of PDEs can be differentially inhibited with pharmacological agents. (See, par. 8 of the 2nd Lerner Declaration).

As aforesaid, Applicant taught in the specification that the class of such specific PDE4 inhibitors could be used, defined it, and exemplified it with two examples coming within and one compound not coming within. Accordingly, there is an adequate written description of the class of specific PDE4 inhibitors that one can use. (See, par. 9 of the 2nd Lerner Declaration).

As a result, based both on the specification and the general knowledge in the at prior to September 24, 1998 a skilled artisan would have known what kind of inhibitors were specific PDE4 inhibitors and what were not. (See, par. 10 of the 2nd Lerner Declaration).

Accordingly, in view of the above, Applicant respectfully submits that the claims 1-7 and 16 fully comply with 35 U.S.C. 112, first paragraph, written description requirement and that the rejection should be withdrawn.

The Examiner also rejected claims 1-7 and 16 as allegedly not complying with 35 U.S.C. §112, first paragraph, enablement requirement. The Examiner contended that the specification is not enabled for use of any and all specific inhibitors of Type 4 adenosine monophosphate phosphodiesterase in treatment of CLL.

Applicant respectfully disagrees and submit that the rejection be withdrawn for the following reasons.

Applicant respectfully submits that a similar alleged lack of enablement rejection was raised in an earlier Office Action mailed November 1, 2004 and specifically addressed in the Amendment and Declaration by Dr. Lerner submitted on March 21, 2005. As a result, the Examiner withdrew this rejection stating that:

> In view of the [First] Lerner Declaration and Applicants' argument that members of the class of PDE4 inhibitors behave alike in a wide range of functional assays and in their use to treat different conditions, this rejection [35 U.S.C. 112, first paragraph enablement] of record is withdrawn. (See, page 2, last par., Office Action mailed on July 25, 2005)

The 2nd Lerner Declaration further addresses this issue.

The First Declaration of Dr. Lerner established that members of the class of PDE4 inhibitors behave alike in a wide range of functional assays. Thus, showing two working examples of compounds taught the skilled artisan that the method works. Dr. Lerner explained that Rolipram, which was one of the exemplified compounds described in the specification, is referred to as a prototypical PDE4 inhibitor. This means that people in the field view results obtained by using it as representative for results obtained using other specific PDE4 inhibitors.

The 2nd Lerner Declaration showed that three additional specific PDE4 inhibitors all worked in treating CLL (See, pars. 15 – 17 of the 2nd Lerner Declaration). Table 2 of Teixeira et al. describes in detail a number of well known PDE4 inhibitors, and confirms their functional similarity to Rolipram, namely, that they all specifically inhibit PDE4. (See, par. 12 of the 2nd Lerner Declaration).

Dr. Lerner tested a second specific PDE4 inhibitor Ro20-174 in the specification. His studies with that PDE4 inhibitor, Ro20-174, confirmed the finding with Rolipram. The data for both of these PDE4 inhibitors are included in the specification. (See, par. 13 of the 2nd Lerner Declaration).

These results have been further confirmed by further studies of the treatment of CLL.

Dr. Lerner co-authored an article confirming that two additional PDE4 inhibitors work about as effectively as Rolipram. These studies confirm what was already described in the specification that the broad class of specific PDE4 inhibitors is effective in treatment of CLL. (See, par. 15 of the 2nd Lerner Declaration). A fifth specific PDE4 inhibitor was also tested and behaved like the other four.

The teaching of the specification has been confirmed with 5 different specific PDE4 inhibitors. (See, par. 17 of the 2nd Lerner Declaration).

The Examiner contended that the experimental evidence based on the two examples described in the specification, namely Rolipram and Ro20-174, would not have allowed the skilled artisan to accept that all PDE4 inhibitors could be predictably used as a treatment for CLL in human patients. The prior Examiner looking at the information provided in the First Declaration of Dr. Lerner agreed with Dr. Lerner and found the specification enabling. While the Examiner contends that "the specification provides no direction or guidance for determining the particular administration regimens (e.g., dosages, timing, administration, etc.) necessary to treat CLL", the Examiner is ignoring the specification, the teaching of the art and the level of expertise of the skilled artisan.

Accordingly, Applicant respectfully disagrees with the Examiner. As stated by Dr. Lerner, a skilled medical doctor who has experience in treating CLL, like Dr. Lerner, would take

into consideration all the factors as indicated in the specification in section C from page 7 to 11 for adjusting dosages, timing and administration routes for any new medicines, including the broad group of PDE4 inhibiting agents. (See, par. 21 of the 2nd Lerner Declaration).

Moreover, the skilled artisan would look to the well known uses of Rolipram as anti-inflammatory agents and as antidepressants, referred to, for example on page 24, lines 8-14 to determine suitable dosage ranges. Further, the skilled artisan would also be able to determine useful dosage ranges from the published information regarding other specific PDE4 inhibitors based upon the information provided for Rolipram. (See, par. 22 of the 2nd Lerner Declaration). These are simple modifications known to the skilled artisan.

Accordingly, Applicant respectfully submits that claims 1-7 and 16 fully comply with 35 U.S.C. §112, enablement requirement and that that rejection should be withdrawn.

In view of the foregoing, Applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the Commissioner is authorized to charge Nixon Peabody LLP Deposit Account No. 50-0850.

Respectfully submitted,

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